LINKAGE IN PEROMYSCUS

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STUDENTS of Mendelism are beginning to display the same interest in possible homologies between the genetic factors or "genes" of different species of animals or plants which the morphologists of thirty years or more ago did in homologies between organs. In considering a given case of suspected homology between genes, two criteria are, so far as I know, employed: (1) Resemblance between the developed characters which are attributed to the action of supposedly homologous genes. Mere similarity of appearance, however, is recognized as an extremely fallible criterion of homology here as in the case of comparative anatomy. (2) Agreement between the "cross-over" value shown by a pair of linked factors in one species, as compared with the corresponding value shown by supposedly homologous factors in another species. If both of the two linked genes under consideration are found to have much the same somatic effects in the two species, and if, furthermore, the degree of linkage is approximately the same in the two cases, the argument is strong for a twofold homology.

Metz[1] and Sturtevant[2] have been investigating the parallel mutations of several species of *Drosophila,* and it is not unlikely that this genus will furnish the best material for the study of genic homologies, just as it has shown incomparable superiority for certain other lines of genetic research.

For rodents, what appear to be parallel mutations have been shown to occur among numerous species, even ones

[1] *Genetics,* March, 1918.

[2] *Genetics,* January, 1921.

belonging to widely different families.[3] In one case, that of the mutation known as "pink-eye," not only is the visible modification closely similar in rats and mice, but the linkage relations between this factor and that for albinism are known to be of the same order of magnitude in the two animals.[4]

Some years ago, Castle[5] described two similar mutations in the Norway rat, which he termed "pink-eyed yellow" and "red-eyed yellow," respectively. These, according to the published descriptions, differ chiefly in the color of the eyes, the latter variety having darker eyes than the former. These two mutations, and likewise true albinism, were all found to result from the modification of distinct genetic factors. Any two of them, when crossed, gave rise to the wild type in the first hybrid generation. On the other hand, further breeding tests led Castle to conclude that all three of these factors were linked. When red-eyed and pink-eyed rats were interbred, the cross-over percentage proved to be about 18. When pink-eyed rats were crossed with albinos, this value proved to be about 21. On the other hand, the linkage between red-eye and albino proved to be almost absolute. One hundred and sixty F_2 albinos and 57 F_2 red-eyed yellows, when mated with pure red-eyes and albinos, respectively, yielded but a single offspring which was not of the wild type.

More recently Dunn[6] has tested the linkage between this same red-eyed condition and albinism in the rat. From his own data he computes a cross-over value of 1.8 per cent., but when his data are combined with those of Castle, this value falls to less than one per cent.

Castle and Dunn have likewise tested the degree of linkage between "pink-eye" and albinism in the mouse

[3] Dunn has compiled these cases in a useful article in the *Journal of Mammalogy*, August, 1921.

[4] According to Castle, the percentage of cross-overs is 21 for rats and 14 for mice. This may or may not be construed as evidence of "homology."

[5] AMERICAN NATURALIST, February, 1914; *Science*, August 6, 1916 (with Wright); Carnegie Institution Publications 241 and 288.

[6] *Genetics*, May, 1920.

(*Mus musculus*). The proportion of cross-overs was found to be about 14 per cent.

Some five years ago I described a pale, red-eyed mutant of *Peromyscus*,[7] which originated among the offspring of three sibs in the F_2 generation of a cross between *P. maniculatus rubidus* and *P. m. sonoriensis*. Since I have already described this "mutant" race rather fully, and since it will again be discussed shortly in a paper by Mr. H. H. Collins and myself, I need not enter into a detailed account of it here. I have not seen specimens of the "red-eyed yellow" rats described by Castle, but I find little in the description of that race which is at all at variance with my own "pallid" race of *Peromyscus*. The latter has undergone a great reduction of the black pigment, while the yellow pigment has been little if any affected. The eyes are commonly dark red, rather than pink, though they present a considerable degree of variability, ranging from a condition not much darker than the true pink of albinos to a condition not much paler than the normal. There are, however, no real intergrades between the pallid mice and the wild type, and the behavior of this complex of characters in crosses is that of a simple monohybrid recessive. Furthermore, it is not an allelomorph of albinism, since the wild type alone results from matings between albinos and pallids.

I have recently carried out tests of the linkage relations between this factor and that for albinism.[8] Thus far, it has not been found practicable to devote any considerable proportion of my time to this phase of the subject, and the numbers are accordingly inadequate for any exact measurement of cross-over values. They are, none the less, sufficient to show the existence of a high degree of linkage between these factors. The number

[7] *Genetics*, May, 1917; AMERICAN NATURALIST, August–September, 1918. This mutant was at first referred to as a "partial albino"; later the noncommittal term "pallid" was applied to it.

[8] The albinos used were all derived from a single brood belonging to the subspecies *Peromyscus maniculatus gambeli*.

of F_2 individuals derived from simple F_1 x F_1 matings is too small to give a representative dihybrid ratio. The really important tests have been made with "extracted" albinos and pallids of the F_2 generation.

Matings have been made (1) between "extracted" albinos and "pure" pallids (*i.e.*, those known to be free from the factor for albinism), (2) between extracted pallids and pure albinos, and (3) between extracted pallids and extracted albinos. There were likewise a number of matings in which the pedigrees were less simple.[9] On the assumption of a wholly independent segregation of these factors, our F_2 pallids (of simple pedigree) should have a 2/3 chance of being heterozygous for albinism, while our F_2 albinos should have a 3/4 chance of being either homozygous or heterozygous for pallid.[10]

Eighteen F_2 mice were involved in these tests. The total number of offspring derived from these was 135, the number per parent ranging from 3 to 26. By no means all of these parents, taken singly, have thus far given birth to a sufficient number of young to prove their genetic composition with any certainty. But the cumulative testimony of all of these matings is overwhelming. Not a single pallid mouse and only two albinos have appeared among the 135 young which have thus far been born. Had there been a normal proportion of "carriers" among the parents, these matings should have yielded 37 albinos and 18 pallids, as the most probable "expected" numbers. That all of the offspring with two exceptions (these being sibs) were of the wild type is evidence of a high degree of linkage (in this case "repulsion") between the albino and the pallid factors.[11]

[9] Back-crosses and heterozygous albinos figured in some of these pedigrees. In these cases the odds are different from those which hold for individuals derived from the simpler types of mating. They have, however, been computed for every animal used. In about half of the "extracted" albinos, for example, there was only a 5/8 chance that the individual carried the pallid factor.

[10] It is a safe assumption that the double recessive form would be albino.

[11] It might be supposed that the testimony of 18 parent mice, even if all of these were shown conclusively to be lacking in "cross-over" gametes,

From these considerations we may regard it as not unlikely that my "pallid" race of *Peromyscus* has resulted from the mutation of a genetic factor homologous with that which has mutated in the case of Castle's "red-eyed yellow" rats.

This decisive result, as regards the existence of linkage between the pallid and albino factors in *Peromyscus,* stands in contrast with the apparent absence of such linkage in another cross between mutant strains of these mice. Albinos were mated with mice belonging to a strain which I have elsewhere referred to rather inappropriately as "yellows."[12] The latter vary from clay color to a distinctly reddish hue, according to the strain, and are characterized primarily by a marked increase in the length of the "agouti" cross-band and by a decrease in the proportionate number of all-black (unbanded) hairs in the pelage. Where present, however, the black pigment is of full intensity. This applies to the basal zone of the body hairs, both dorsal and ventral, to the black hairs of the dorsal tail stripe, as well as to the eyes, ears and soles of the feet.

Matings between albinos and "yellows" have resulted exclusively in F_1 mice of the wild type (dark). An F_2 generation of 83 was obtained, consisting of 52 dark individuals, 13 yellows and 18 albinos. On the assumption of purely random assortment of gametes, the "expected" numbers are 44, 15 and 20, respectively. The observed numbers are doubtless within the range of "accidental" variability. In any case they give no evidence

would not be sufficient to prove the existence of linkage. It should be repeated, however, that we are not here dealing with cases in which there would be merely an equal chance of combining the two mutant factors in the same individual. The odds in favor of this (linkage aside) may, as stated above, be as high as 2 to 1, or even 3 to 1. Thus, the likelihood of obtaining, by chance alone, 17 non-cross-over cases out of 18 becomes vanishingly small.

[12] *Genetics,* May, 1917; AMERICAN NATURALIST, August–September, 1918. A more complete account of these mice, dealing with two subvarieties differing somewhat in color, is included in a forthcoming paper by Mr. H. H. Collins and myself.

of linkage, the occurrence of which would have reduced the proportionate number of dark individuals, instead of increasing it.

The number of F_2 albinos and yellows which have been thus far tested is very small, but it is of interest that the proportion of recombinations is even greater than would be expected from random assortment. Inclusion of these meager results in the present report seems justified by the probability that we shall not soon rear any considerable number of hybrids between the yellow and albino varieties.

Seven extracted albinos have been mated with pure yellows. Three of these have given only yellow offspring, the numbers being 9, 13 and 21, respectively. Thus, three of these seven albinos are, in all probability, double recessives (*ccyy*). (One in four should be double recessives, according to chance.) Three other albinos have given mixed offspring. They are evidently of the formula *ccYy*. The remaining one appears to have the formula *ccYY*, as judged by the production of 15 dark young.

Two extracted yellow females mated with a (supposedly) pure albino male gave birth to 4 albinos and 4 dark.[13] No albinos would be expected here if linkage were complete, while only one third should be albinos in the total absence of linkage. Thus the number of recombinations is again too high, even on the assumption of no linkage.

These numbers are, of course, very small. But even here such proportions would have been quite improbable had any marked degree of linkage existed—such, for example, as has been found to exist between the pallid and albino factors.

[13] It is only fair to add that 4 yellows likewise resulted from these matings. This was doubtless due to the fact, unsuspected at the time, that the albino male carried the "yellow" factor, one of his *two* great-grandparents having been heterozygous for yellow.